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A Design of Boron Neutron Capture Therapy for Cancer Treatment in Indonesia

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Abstract-A design of boron neutron capture therapy for of cancer treatment in Indonesia. Boron Neutron Capture Therapy (BNCT) is an advanced form of radiotherapy technique that is potentially superior to all conventional techniques for cancer treatment, as it is targeted at killing individual cancerous cells with minimal damage to surrounding healthy cells. After decades of development, BNCT has reached clinical-trial stages in several countries, mainly for treating challenging cancers such as malignant brain tumors. The Indonesian consortium of BNCT already developed of the design BNCT for many cases of type cancers using many neutron sources. The main objective of the Indonesian consortium BNCT are the development of BNCT technology package which consists of a non nuclear reactor neutron source based on cyclotron and compact neutron generator technique, advanced boron-carrying pharmaceutical, and user-friendly treatment platform with automatic operation and feedback system as well as commercialization of the BNCT though franchised network of BNCT clinics worldwide. The Indonesian consortium BNCT will offering to participate in Boron carrier pharmaceuticals development and testing, development of cyclotron and compact neutron generators and provision of neutrons from the 100 kW Kartini Research Reactor to guide and to validate compact neutron generator development. Studies were carried out to design a collimator which results in epithermal neutron beam for Boron Neutron Capture Therapy (BNCT) at the Kartini Research Reactor by means of Monte Carlo N-Particle 5 (MCNP5) codes. Reactor within 100 kW of output thermal power was used as the neutron source. The design criteria were based on the IAEA's recommendation. All materials used were varied in size, according to the value of mean free path for each. Monte Carlo simulations indicated that by using 5 cm thick of Ni as collimator wall, 60 cm thick of Al as moderator, 15 cm thick of ^{60}Ni as filter, 1,5 cm thick of Bi as γ-ray shielding, 3 cm thick of $^{6}Li_2CO_3$-polyethylene as beam delimiter, with 3-5 cm varied aperture size, epithermal neutron beam with minimum flux of 7,8 x 10^8 n.cm^{-2}.s^{-1}, maximum fast neutron and γ-ray components of, respectively, 1,9 x 10^{-13} Gy.cm^2.n^{-1} and 1,8 x 10^{-13} Gy.cm^2.n^{-1}, maximum thermal neutron per epithermal neutron ratio of 0,009, and beam minimum directionality of 0,72, could be produced. The beam did not fully pass the IAEA's criteria, since the epithermal neutron flux was still below the recommended value, 1,0 x 10^9 n.cm^{-2}.s^{-1}. Nonetheless, it was still usable with epithermal neutron flux exceeded 5 x 10^8 n.cm^{-2}.s^{-1}. When this collimator was surrounded by 8 cm thick of graphite, the characteristics of the beam became better that it passed all IAEA's criteria with epithermal neutron flux up to 1,7 x 10^9 n.cm^{-2}.s^{-1}. it is still feasible for BNCT in vivo experiment and study of many cases cancer type i.e.; liver and lung curcinoma. In this case, thermal neutron produced by model of Collimated Thermal Column Kartini Research Nuclear Reactor, Yogyakarta. Sodium boroncaptate (BSH) was used as in this research. BSH had effected in liver for radiation quality factor as 0.8 in health tissue and 2.5 in cancer tissue. Modelling organ and source used liver organ who contain of cancer tissue and research reactor. Variation of boron concentration was 20, 25, 30, 35, 40, 45, and 47 µg/g cancer. Output of MCNP calculation were neutron scattering dose, gamma ray dose and neutron flux from reactor. Given the advantages of low density owned by lungs, hence BNCT is a solid option that can be utilized to eradicate the cell cancer in lungs. Modelling organ and neutron source for lung carcinoma was used Compact Neutron Generator (CNG) by deuterium-tritium which was used is boronophenylalanine (BPA). The concentration of boron-10 compound was varied in the study; i.e. the variations were 20; 25; 30; 35; 40 and 45 µg.g-1 cancer tissues. Ideally, the primary dose which is solemnly expected to contribute in the therapy is alpha dose, but the secondary dose; i.e. neutron scattering dose, proton dose and gamma dose that are caused due to the interaction of thermal neutron with the spectra of tissue can not be simply omitted. Thus, the desired output of MCNPX; i.e. tally, were thermal and epithermal neutron flux, neutron and photon dose. The liver study variation of boron concentration result dose rate to every variation were0,042; 0,050; 0,058; 0,067; 0,074; 0,082; 0,085 Gy/sec. Irradiation time who need to every concentration were 1194,687 sec (19 min 54 sec);999,645 sec (16 min 39 sec); 858,746 sec (14 min 19 sec); 743,810 sec (12 min 24 sec); 675,156 sec (11 min 15 sec); 608,480 sec (10 min 8 sec); 585,807sec (9 min 45 sec). The lung carcinoma study variations of boron-10 concentration in tissue resulted in the dose rate of each variables respectively were 0.003145, 0.003657, 0.00359, 0.00385, 0.00438 and 0.00476 Gy.sec-1 . The irradiated time needed for therapy for each variables respectively were 375.34, 357.55, 287.58, 284.95, 237.84 and 219.84 minutes.

Keywords — liver, Lung carcinoma, Boron Neutron Capture Therapy, Compact DT Neutron generator.

INTRODUCTION

Cancer was a leading cause of death worldwide, accounting for 7.6 million deaths (around 13% of all deaths) in 2008. Lung, stomach, liver, colon and breast cancer caused the most cancer deaths each year. Liver cancer was in third position (695.000 death) as cause of death after lung and stomach cancer [1]. Indonesia requires a technique of handling and treatment of cancer is safe and effective. Secure here means the destruction or adverse events received by healthy organs was minimal. The skin is the body part that is closest to the radiation source so that the dose received was also greater than in tumors of organs in the body. Due to these side effects, do not allow exposure only from one direction only. This side effect has been reduced by multiplying the direction of irradiation (radiation field) to more than one. The dose received by the skin surface will be less than using radiation field slightly but side effects such as the appearance of a blackish color of the skin is still there. Surface dose reduction by increasing the radiation field aims to secure critical organs around the area of irradiation. Therefore, until now the external radiation is used because it is still able to treat and control the growth of cancer cells. Effective means the dose received by the cancer cells as much as possible until adequate to treat and control the growth. Effective here cannot be separated from the safe limit [2].

In ensuring that there is cancer in the patient's body controlled or killed, the need for determining the value of the collective radiation received by the cancer cells. Dose values are based on the value of the Linear Energy Transfer (LET) of each of the radiation used and the material traversed by the radiation. This value can be called absorbed dose. According to BAPETEN Decree number 4 in 2013, "The radiation dose is the amount of radiation contained in the radiation field or total radiation energy absorbed or received by the material in its path ". Calculation of dose can also be called dosimetry. Boron Neutron Capture Therapy was cancer therapy who used physics principle in nuclear reaction interaction. Interaction occurred when stable boron (boron-10) were irradiated by low energy neutron (thermal neutron). Main reaction was occurred in this therapy based on Equation (1) and (2) [3].

$$[^{10}_{5}B] + [^{1}_{0}n] \rightarrow [^{11}_{5}B]^{*} \rightarrow \begin{cases} [^{4}_{2}He] + [^{7}_{3}Li] + 2.79\ MeV & (6.1\%) \\ [^{4}_{2}He] + [^{7}_{3}Li]^{*} + 2.31\ MeV & (93.9\%) \end{cases} \quad (1)$$

$$[^{7}_{3}Li]^{*} \rightarrow [^{7}_{3}Li] + \gamma\,(0{,}48MeV) \quad (2)$$

In TRIGA MARK-II type research reactor in Yogyakarta, which has also been known as Kartini Research Reactor, the facility for BNCT is going to be built for an advanced study which uses tumour-injected animals as the object. The thermal column of this reactor is planned to be implanted with a device which is capable of narrowing the neutron beam, called as *collimator*. Due to the tendency of epithermal neutron beams usage for BNCT, the collimator must contains materials needed to produce epithermal neutron beam which fulfill some particular characteristics recommended by the International Atomic Energy Agency (IAEA). Thus, a proper collimator has to be designed. Liver cancer was malignant who located in liver. It had a primary tumor in liver and could be called by primary liver cancer or *Hepatocellular Carcinoma* (HCC). HCC had a different condition if liver cancer caused by metastatic from the cancer in other organ such as breast cancer, lung cancer or colon cancer. This condition called as Metastatic liver cancer [4].

Two boron compounds that have been used for BNCT is BSH (sodium Boroncaptate) and BPA (boron phenylalanine). Both of these

compounds have accumulated difference of place when inserted into the body. BSH will accumulate in the cell membrane while the BPA will accumulate in the nucleus of cells [5]. Liver was given an infusion sodium boroncaptate (BSH) by intracarotidly (i.c.) method. Intracarotidly is infusion of boron compound thoroughly internal artery in carotid gland. Carotid gland is artery who supply blood into head and neck. Liver was irradiated in nuclear reactor until the target get dose enough and did not get over dose in health tissue [3]. Concentration values for the patients was 47 ppm in tumor tissue (CT patients) and 8 ppm in healthy liver tissue (CR patients) . In rodents (rats) , the peak concentration of boron - 10 in the liver occurs when two hours after injection into the body, Sodium boroncaptate (BSH) was used as in this research. BSH had effected in liver for radiation quality factor as 0.8 in health tissue and 2.5 in cancer tissue [6].

THEORY

Table 1 shows the beam criteria recommended by the IAEA. The energy limits of 5 x 10^{-7}, 0,01, and 20 MeV were used which, respectively, denoted the energy range for thermal, epithermal, and fast neutrons. In this table, Φ_{epi}, Φ_{th}, and J are epithermal neutron flux, thermal neutron flu , and eutron current, respectively. Moreover, $\dot{D}_f$ and $\dot{D}_\gamma$ stand for dose rates due to the fast neutrons and gamma rays.

Table 1. Beam criteria recommended by the IAEA [7]

Nomenclature	Value
Φepi (n.cm^{-2}.s^{-1})	> 1,0 x 10^{9}
$\dot{D}_f / \Phi_{epi}$ (Gy.cm^2.n^{-1})	< 2,0 x 10^{-13}
$\dot{D}_\gamma / \Phi_{epi}$ (Gy.cm^2.n^{-1})	< 2,0 x 10^{-13}
Φ_{th} / Φ_{epi}	< 0,05
J / Φ_{epi}	> 0,7

Several experiences in designing collimator for BNCT have been conducted both based on the materials selection and the geometry optimisation. A collimator consists of 5 components: collimator wall, moderator, filter, γ-ray shielding, and aperture.

Collimator wall should reflect neutrons back into the inner part of collimator. Suitable reflector materials for this are those with high scattering cross section and high atomic mass, such as Pb, Bi, PbF_2, and Ni. Moderation of fast neutrons is best accomplished by low atomic mass materials. Suitable candidates are Al, C, S, Al_2O_3, AlF_3, D_2O, and $(CF_2)n$. Materials such as Pb and Bi may be placed in the beam to reduce γ-rays. These will nonetheless reduce neutron beam intensity. For epithermal neutron beams, it is desirable to limit thermal and fast neutron contamination by filtering. Filter materials for thermal neutrons require ^{6}Li, ^{10}B or Cd. For filtering out the fast neutrons, ^{60}Ni isotope can be placed. Aperture is a part of collimator which provides required cross section of the beam. This part is made of $^{6}Li_2CO_3$-polyethylene or B_4C. Epithermal neutrons striking the wall of the collimator are thermalised and captured. James Michaelson (2003) used screening mammography to detect breast cancer. According to the result of the study, it was found that the size at which breast cancers become surely detectable was approximately 30 mm. Thus, 30 mm would be a convenient minimum aperture size for the collimator design [7,8,9].

BNCT is based on the reaction of low energy neutrons with boron-10 producing two high particles: a lithium-7 ion and an alpha particle. The cross section of the 10B(n,α)7Li reaction is very high: 3837 barn at thermal energies,and the Q-value is 2.790 MeV. With a probability of 94%, the reaction gives rise to

the Li ion in an excited state, which returns to its fundamental level with a gamma emission of 478 keV [10]. First of all, a boron-10 carrying drug is injected into the blood. Then, a tumor accumulates the drug through the blood transportation system. Thereafter, the tumor is irradiated by a thermal neutron; i.e. E ≈ 0.025 eV or an epithermal neutron; i.e. 1 eV < E < 10 keV source. Finally, the boron-10 atoms inside the tumor capture the neutrons to produce highly energetic helium-4 nuclei; i.e., alpha particles and recoiling lithium-7 ions to kill the tumor cells [10].

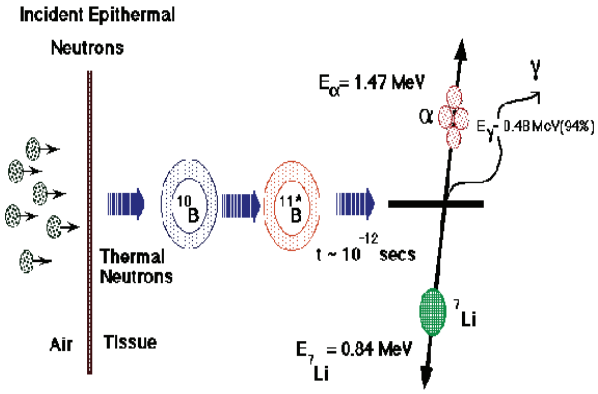


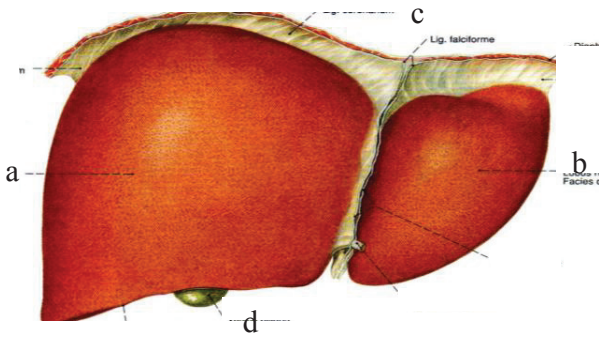
Figure 1. Schematic of Boron-10 and neutron interaction [4].

There are three major components which are required in BNCT; i.e. boron compounds, neutron source and dosimetry of BNCT. Two typical boron compounds which are commonly used for BNCT are sodium borocaptate (BSH) and p-boronophenylalanine (BPA). Both are currently tested in on-going clinical trial since 2011 and has been through pre-clinical trial notably in Brookhaven National Laboratory, USA. One of the compounds, BSH will not take up into normal brain cells because of the Blood Brain Barrier (BBB) effect. BBB is highly selective permeability barrier that separates the circulating blood from the brain extracellular fluid (BECF) in the central nervous system (CNS). Although BBB of tumor cell is damaged so that BSH is able to accumulate in tumor cell, especially around the cell membrane. The other boron compounds, BPA has different characteristic. Its chemical structure resembles tyrosine and dihydroxy-phenylalanine (DOPA) which is the precursor of the melanin metabolism. Its characteristic makes BPA has inherent accumulation around the cell nucleus [7,8,9].

There are 4 main doses that contribute in the treatment of BNCT: the boron dose from boron neutron capture reaction, the proton dose from nitrogen capture reaction, the neutron dose and the gamma dose. The primary dose is the dose of Lithium-7 and alpha with energy of 2,79 MeV (6,1%) and 2,31 MeV (93,9%). Lithium-7 produced from the decay reaction will back to the initial energy level and emit gamma (0,48MeV). The average energy produced from the interaction of the Boron-10 with thermal neutrons is 2,33 MeV. The secondary dose comes from 3 interactions. Interaction between fast and thermal neutron with tissue commonly called neutron scattering. The calculated dose is the dose of neutron scattering due to the reaction between fast and thermal neutron with Hydrogen-1 nuclei. Protons are recoil product in the interaction. Gamma and hydrogen-2 are produced from absorption reaction of the neutron interaction with hydrogen contained in the body tissues. Produced hydrogen-2 is an excited atom. hydrogen-2 production rate of thermal neutron interaction with hydrogen-1 is proportional to the photon release rate with energy of 2,33 MeV.Nitrogen-14 has a fairly high mass fraction which is 4,5% of the tissue mass. Tissue irradiation by thermal neutron leads to interaction of thermal neutrons with nitrogen-14. This reaction produces carbon-14 and proton with energy of 0,66 MeV. Carbon-14 is a radioactive element with a long half-life which is 5730 years.

METHOD

This study was conducted by doing simulations using MCNP5 program. It works based on the probability of interactions between radiations and materials which is derived from the microscopic cross sections. The probability is defined as the ratio of microscopic cross sections of interaction of interest per total microscopic cross sections. Thus, every interaction has its probability. The individual probabilistic events that comprise a process are simulated sequentially. The probability distributions governing these events are statistically sampled to describe the total phenomenon. The statistical sampling process is based on the selection of random numbers. [6]



Description: a. right lobe b. left lobe c. diaphragms d. bile

Figure 2. Liver Part diaphragm maintained to show the merging of the heart and diaphragm. Source: (Robins, 2003)

Figure 2. is used for modeling the liver. Regional cancer network consists of Clinical Tumor Volume (CTV) and Planning Tumor Volume (PTV) and conducted modeling using mathematical equations. Cancer tissue waslocated in the right lobe. Interaction from neutron and matter in liver tissue could be calculated to several dose component. The component was obtain from recoil and photon. Interaction from fast or epithermal neutron and tissue matter was showed in Equation (3) (Rorer et al, 2001).

$$ {}_{1}^{1}H + {}_{0}^{1}n \longrightarrow {}_{0}^{1}n' + {}_{1}^{1}p \qquad (3) $$

Dose from scattering interaction from fast and epithermal neutron with hydrogen would be calculated in this research as scattered neutron dose (Rorer et al, 2001).

$$ {}_{1}^{1}H + {}_{0}^{1}n\,(0{,}0025\ eV) \rightarrow {}_{0}^{1}D + \gamma\,(2{,}22\ MeV) \qquad (4) $$

Gamma dose from Equation (4) would be calculated in this research as dose from thermal neutron and hydrogen reaction.

Formula (1) explained interaction from thermal neutron and boron-10. Energy of alpha and lithium who produced by adsorption interaction was 2.33 MeV (Rorer et al, 2001).

$$ {}_{7}^{14}N + {}_{0}^{1}n(0{,}0025\ eV) \rightarrow {}_{6}^{14}C + {}_{1}^{1}p \qquad (5) $$

Dose from proton who produced from interaction from thermal neutron and nitrogen-14 will be calculate based on Formula (5). Dose in BNCT occurred belongs to neutron interaction to liver tissue. The interaction who take effect in dose calculation for this research was (Mika, 2002):

1. Boron reaction dose.
2. Scattered neutron dose.
3. Gamma dose.
4. Proton dose.

Formula who used for dose calculation in BNCT based on Equation (6).

$$ \dot{D}_{total} = (w_{Alfa} \times \dot{D}_{Alfa}) + (w_p \times \dot{D}_{proton}) + (w_n \times \dot{D}_{neutron}) + (w_\gamma \times \dot{D}_\gamma) \qquad (6) $$

remark:

$\dot{D}_{boron}$: dose rate for boron interaction
w_{boron} : biological weight factor for boron interaction
$\dot{D}_{proton}$: dose rate for proton

w_p : biological weight factor for proton
$\dot{D}_{neutron}$: dose rate for neutron
w_n : biological weight factor for neutron scattering
$\dot{D}_\gamma$: dose rate for gamma
w_γ : biological weight factor for gamma

Monte Carlo method is a probabilistic approach to the possibility of interactions that will occur in radiation. Monte Carlo specify the desired value by performing simulations of each particle and noted that according to the characteristics of the particles and the medium through which it passes. Monte Carlo methods only show the information in accordance with the tally desired by the user (Thomas et al, 2003). Derived from the neutron source reactor Kartini after passing a special collimator BNCT and have characteristics such as Table 1.

Based on Table 2, all of parameter who used in thermal column Kartini research reactor accepted from the IAEA Recommendation. This study was conducted by doing simulations using Monte Carlo N-Particle eXtended (MCNPX) program. It works based on the probability of interactions between radiations and materials which is derived from the microscopic cross sections. The individual probabilistic events that comprise a process are simulated sequentially. The probability distributions governing these events are statistically sampled to describe the total phenomenon. The statistical sampling process is based on the selection of random numbers [7].

RESULT AND DISCUSION

Intended use of the thermal column because it already meets the IAEA recommendations on the use of BNCT facility neutron output. Liver is placed in the thermal column of the right lobe position in aperture collimator. Aperture used is 5 cm. The distance between the organ and the wall collimator 0.5 cm. Simulation heart is divided into four major sections. The outer part of the network consists of a healthy liver is composed of two lobes. Lobes modeled into two lobes, namely the right lobe and left lobe. Tumor tissue found on the right lobe. The second part of the volume of tissue called tumors planning (PTV). PTV has the same material with healthy tissue. The third part of a network called the clinical tumor volume (CTV). CTV has the characteristics of a material similar to the tumor due to the persistence of tumor infiltration of the tumor area. The density has the same value but the amount of tumor tissue distribution of boron in tumor tissue sections CTV half innermost part consists of cancerous tissue or could be

Table 2. Beam Characteristic in BNCT Facility, Source: (Nina, 2013)

Parameter	Notation (Unit)	IAEA Recommendation	Result.
Epithermal neutron flux	$\phi_{epi}(n.cm^{-2}.s^{-1})$	> 1,0 X 10^{9}	1,65 x 10^{9}
Ratio of fast neutron dose rate and Epithermal neutron flux	$\dot{D}_f / \phi_{epi}(Gy.cm^2.n^{-1})$	< 2.0 X 10^{-13}	1,59 x 10^{-13}
Ratio of gamma dose rate and epithermal neutron flux	$\dot{D}_\gamma / \phi_{epi}(Gy.cm^2.n^{-1})$	< 2,0 X 10^{-13}	1,16 x 10^{-13}
Ratio of thermal neutron flux and epithermal neutron flux	ϕ_{th}/ϕ_{epi}	< 0,05	0,007
Ratio of neutron current and neutron flux	J/ϕ_{epi}	> 0,7	0,72

called gross tumor volume (GTV). This meets the tumor tissue sections with characteristics in accordance with plans including the number and density of boron. The amount of boron available in certain parts will affect the dose received.

Description:

1. Planning tumor volume (PTV)
2. Clinical tumor volume (CTV)
3. Cancer tissue/gross tumor volume (GTV)

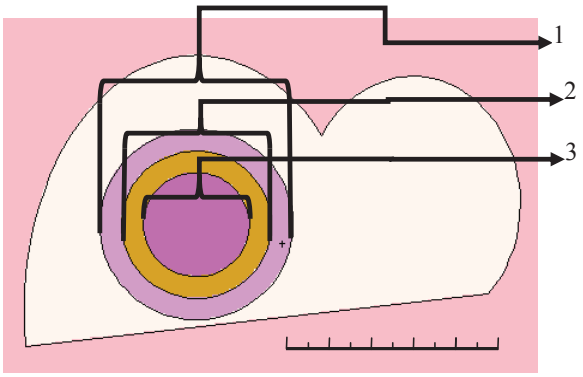


Figure 3. Frontal view of heart with the center point in the tumor mass.

Front piece depicts the shape of heart modeling based on Figure 2. Lobe of the right have larger sizes and there is a cancer in the lobe with a diameter of 5 cm.

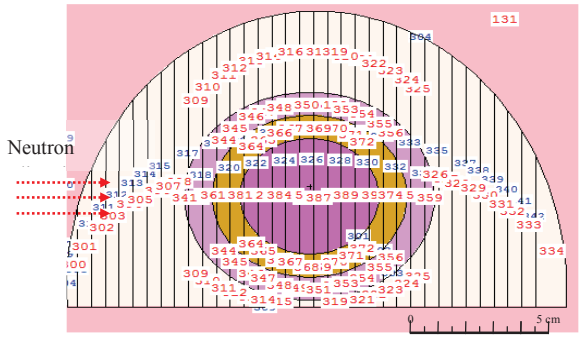


Figure 4. Pieces addition to the liver with a central point in the tumor mass.

Side pieces of the organ showing the lines to divide each area at a specific depth As per the available scale, depth of cancer found in 6 cm to 11 cm. Figures show the number of blue used surface and pink figures indicate cell numbers used in the modeling of the liver . In Figure 2, the modeling approach of the geometry of the heart from the front as listed in Figure 1. The right lobe, the left lobe and the bottom surface of the organ has been approached from the image geometry. Each section is divided into layers with the same thickness of 0.5 cm. Each layer of the neutron flux is analyzed and then the dose is calculated using the equation stated in method section. Dose rate of the layer that includes the area contained cancer is the focus in this study. Dose rate in tissue contained cancer tissue tumors are in the area and CTV

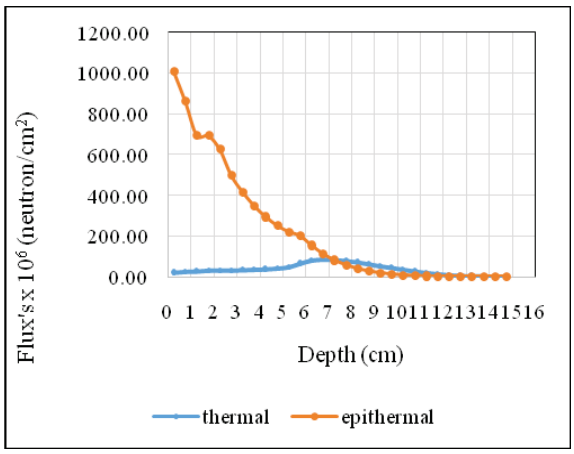


Figure 5. Distribution of neutron in liver tissue.

Figure 5 showed changed of neutron's flux varied with liver depth. Peak of epithermal neutron flux's was gotten in 1.5 cm and decreased after that. Peak of thermal neutron flux was obtained from 5 to 10 cm.

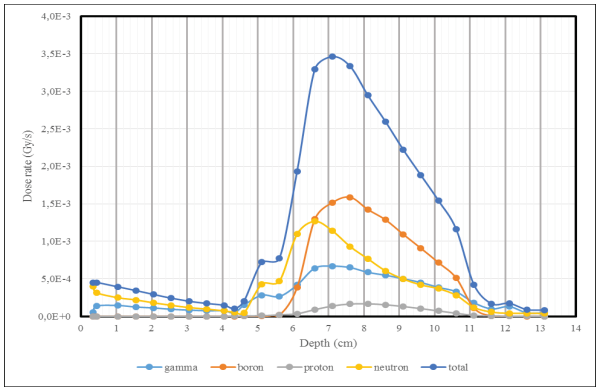


Figure 6. Dose rate distribution in tissue

Figure 6 showed dose rate in irradiated tissue. Normal tissue was obtained from 0 until 5 cm. Maximum dose was obtained in cancer tissue. Liver which suffered cancer from 6 to 11 cm.

Table 3. Dose Rate and Irradiating Time.

Concentration of B-10 (µg/g tumor tissue)	Dose rate in cancer (Gy/s)	Irradiating time(min)
20	0,042	19,911
25	0,050	16,661
30	0,058	14,312
35	0,067	12,397
40	0,074	11,253
45	0,082	10,141
47	0,085	9,763

Table 3 given the dose rate who accepted in cancer tissue. Dose rate can influence irradiating time. Irradiating time is gotten when dose in cancer tissue enough. Cancer need 50 Gy to die.

Table 4. Dose in Health tissue

Concentration of B-10 (µg/g tumor tissue)	Dose in Health Tissue (Gy)
20	5,875
25	5,016
30	4,306
35	3,735
40	3,393
45	3,075
47	2,950

Limit the dose used for liver tissue was 35 Gy (Herman, 2009). Dose received by healthy tissue by Table 4 which passes no dose limiting values of healthy liver tissue. All concentration values in Table 4 can be used for the irradiation of liver cancer.

As in the case of lung carcinoma, the study focused on lung (left lung) as shown in Figure 7. The number in red represents the number of cell cards in Visual Editor (VISED) which implies the organ where the doses were calculated. As mentioned before, the radius of tumor is 3 cm and the tumor divided into 3 regions: the cell number 520 (pinkish region) is PTV which has the radius of 3 cm from the centre point, the cell number 521 (crème region) is CTV which has the radius of 2,5 cm while the cell number 522 (turqoise region) is GTV with the radius of 2 cm. The tumour is located in the centre of the left lung whose depth from the surface (skin) is 6,5 to 8,8 cm. As seen, cell number 7 represents skin, cell number 9 represents left lung, and cell number 29 represents rib cages, while cell number 54, 56, 58 and 60 represent the whole heart.

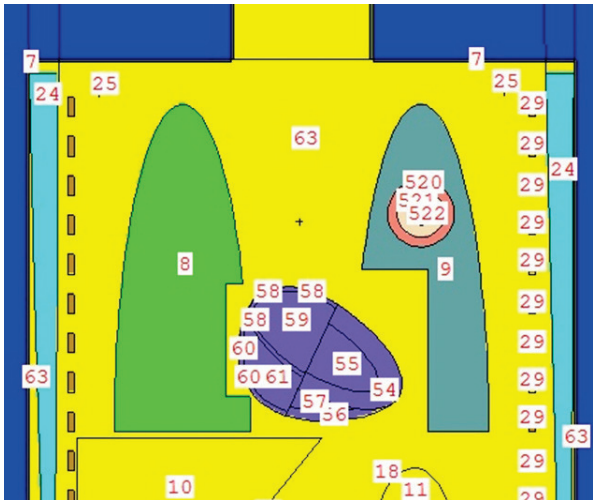


Figure 7. Thorax and lungs of the phantom with the tumour in anterior-posterior view.

Moreover, neutron flux was being calculated in various depth of each cells which represent organs. The result was varied in relation with the depth of the cells with skin as the starting point. Figure 7. depicts the relation between neutron flux and the depth of the cells. The range of energy was defined in the study to differentiate the neutron flux; i.e. thermal and epithermal neutron flux.

Figure 8. shows the neutron flux in the targeted organs. It appears that the neutron flux went smaller cm by cm because the flux interacted with components on the surface and had no much energy left when the neutron flux went deeper. The neutron flux hypothetically

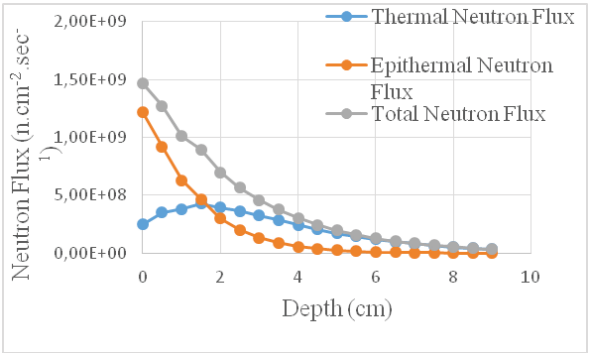


Figure 8. Distribution of neutron flux in various depth of calculated cells.

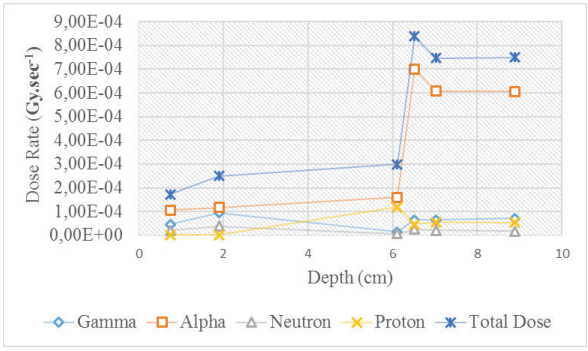


Figure 9. Distribution of dose rate in targeted tissue with concentrated boron-10 of 25 µg.g^{-1} tissue.

was estimated to go smaller to avoid the damage of the cells in targeted organs, especially skin. In the surface; i.e. the depth of 0 cm, the epithermal neutron flux had a greater value than thermal neutron flux because fast neutron was moderated to become in the range of epithermal neutron. The number of thermal neutron flux was well below the epithermal neutron flux due to the energy possessed by thermal neutron had lessen during the process to the tissue. In the deeper depth, the decreasing of thermal neutron flux which was similar to epithermal neutron flux happened due to the scattering interaction with the spectra of tissue. The peak of $f_{epithermal}$ was $4{,}00\times10^{8}$ n.cm^{-2}.sec^{-1}. The result is logic and acceptable regarding to the neutron yield of the conceptual design of Compact DT Neutron Generator is similarly high as the outcome of nuclear research reactor; i.e. around 1×10^{9} n.cm^{-2}.sec^{-1}. The depth of PTV, CTV and GTV from skin consecutively are 6, 51 cm; 7, 08 cm and 8, 88 cm. The peak of thermal neutron flux is in the range of 1,5 to 2 cm. The result is logic and acceptable regarding to the neutron yield of the conceptual design of Compact DT Neutron Generator is similarly high as the outcome of nuclear research reactor; i.e. around 1×10^{9} n.cm^{-2}.sec^{-1}.

Figure 9. depicts the result of dose rate distribution in cells which the neutron radiation passing through and the amount of dose which produced and emitted in the certain duration of interaction with tissue. The radiation passed through skin, rib cages, healthy tissue of lungs to tumor tissue in lung. The peak of dose rate is in the depth range of 5,5 to 8,5 cm where tumor tissue which were divided in to three regions; i.e. PTV, CTV and GTV was located. In figure 9., it appears that the highest contribution of dose rate is the dose rate of alpha which was emitted in the interaction between boron-10 and thermal neutron in tissue. It was hypothetically expected because the solemnly desired contribution of dose in every BNCT treatment was the dose of alpha in tumor tissue.

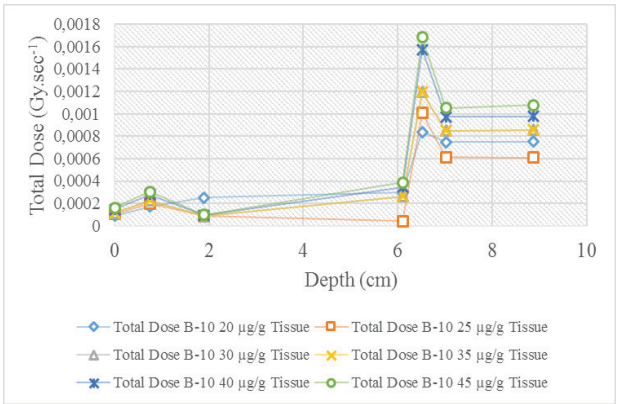


Figure 10. As summary, distributions of total dose rates in concentrated tissue with varied concentrations of boron-10.

Figure 10. can be used as a comparison to figure 9. to ensure that the correlation between depth of the cells and dose rate is persisted

depending on the mass fractions of cells and the concentrations of boron-10. The boron-10 concentration of 20 µg/g tumor tissue resulted in the total dose rate of 0,003145 Gy.sec^{-1}, the concentration of 25 µg/g Gy.sec^{-1} tumor tissue resulted in the total dose rate of 0,003657 Gy.sec^{-1}, the concentration of 30 µg/g Gy.sec^{-1} tumor tissue resulted in the total dose rate of 0,00359 Gy. sec^{-1}, the concentration of 35 µg/g Gy.sec^{-1} tumor tissue resulted in the total dose rate of 0,00385 Gy.sec^{-1}, the concentration of 40 µg/g tumor tissue resulted in the total dose rate of 0,00438 Gy.sec^{-1} while the boron-10 concentration of 45 µg/g tumor tissue resulted in the total dose rate of 0,00476 Gy.sec^{-1}.

Table 5. Dose rate and irradiation time.

Boron Concentration (µg.g^{-1} tissue)	Dose Rate (Gy.sec^{-1})	Irradiation Time (minute)
20	0,00223	375,34
25	0,00233	357,55
30	0,00291	287,58
35	0,00299	284,95
40	0,00352	237,84
45	0,00381	219,84

Table 5. depicts the data of variations in boron-10 concentration resulting in changing of dose rate in tissue (Gy.sec^{-1}) and irradiation time needed (minute).

After gaining the value of dose rate, irradiation time can be obtained by substituting the number in the equation using spread sheet application. The total dose which needs to eradicate lung cancer cells is 50 Gy. Table 5. shows the relation between the dose rate and irradiation time. As showed, the dose rate had effects on irradiation time needed in the treatment to fulfill the desired dose in the tumor. Irradiation time has to ensure the duration of delivering the needed dose to combat and eradicate cancer cell.

Figure 11. depicts the result of the dose rate of varied amount of boron-10 concentration

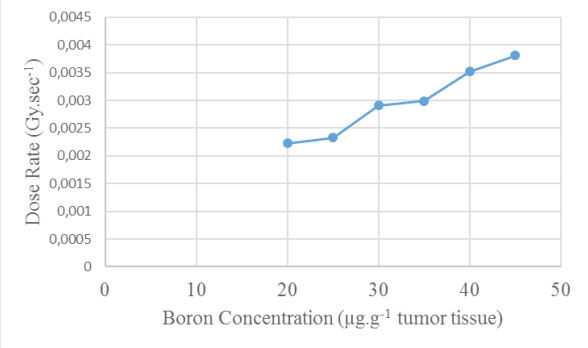


Figure 11. Dose rate in concentrated tumor tissue with varied Boron-10 concentration.

in concentrated tumor. As showed, the dose rate increased simultaneously with the increasing amount of boron-10 concentration in tissue.

In the opposite, figure 12 shows the relation between irradiation times needed in treatment with the varied amount of boron-10 concentration in concentrated tumor. As showed, the irradiation time decreased with the increasing amount of boron-10 concentration in tissue. The range of irradiation time needed for treatment is from 219,84 to 375,34 minutes.

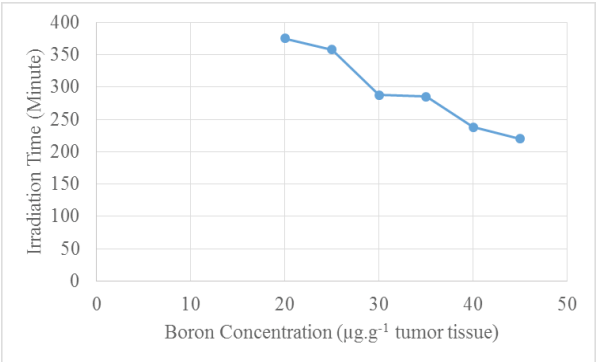


Figure 12. Irradiation time needed in treatment with the varied amount of boron-10 concentration in tumor

The boron-10 concentration of 20 µg/g tumor tissue resulted in irradiation time of 375,34 minutes, the concentration of 25 µg/g Gy.sec^{-1} tumor tissue resulted in irradiation time of 357,55 minutes, the concentration of 30 µg/g Gy.sec^{-1} tumor tissue resulted in irradiation time of 287,59 minutes, the concentration of 35 µg/g Gy.sec^{-1} tumor tissue resulted in irradiation

time of 284,96 minutes, the concentration of 40 μg/g tumor tissue resulted in irradiation time of 237,85 minutes while the boron-10 concentration of 45 μg/g tumor tissue resulted in irradiation time of 219,840 minutes. As showed, irradiation time which need for the treatment decreased along with the increasing amount of boron-10 concentration in tumor tissue. Although the unit of time is quite long, in comparison with traditional therapies such as Co-60, the duration of lung carcinoma treatment by BNCT based on this simulation is far more convenient.

The reduction of irradiation time needed reflects the higher probability of interactions between boron-10 with cancer cell which emits alpha particle. The richer amount of boron-10, the higher possibility of interactions may occur in tissue.

While the tumor was being irradiated, it is not only the tumor region which will be exposed to the radiations, but all organs in the body will also be exposed too due to the secondary interactions. For consideration, it is an obligatory to calculate the dose rate and the amount of dose that may expose the other organs which are located near the targeted tumor. In this case, the organs at risk are skin, rib cages and heart. Every organ has its own Normal Tissue Tolerances, for skin, rib cages and heart respectively are 6 Gy, 6 Gy and 2,5 Gy.

Skin has probability to have erythema, moist desquamation and ulceration as an effect if skin being exposed more than the allowed Normal Tissue Tolerances, while heart could have cardiomyopathy, damage in the valve and premature coronary artery disease once the dose exceed the Normal Tissue Tolerances. The result that was obtained from the equations showed that all variations of Boron-10 concentration results in that all organs at risk were still under their Normal Tissue Tolerances with the biggest value of all three were when the tumor was injected by 45 μg/g tissue with the dose were for skin, rib cages and heart respectively 2,703 Gy, 1,636 Gy and 0,789 Gy. Although all variations of boron-10 concentration were still acceptable, the amount of boron-10 in the body must be limited due to the toxic effect that may be caused after the irradiation.

Table 6. The dose rate of neutron radiation in healthy tissue and Organs at Risk (OAR).

Boron Concentration ($\mu g.g^{-1}$ tissue)	Organ at Risk	Dose (Gy)	Normal Tissue Tolerances (Gy)
20	Skin	4,055	6
	Rib	2,438	6
	Heart	0,789	2,5
25	Skin	3,964	6
	Rib	1,767	6
	Heart	0,715	2,5
30	Skin	3,939	6
	Rib	1,577	6
	Heart	0,667	2,5
35	Skin	3,917	6
	Rib	1,492	6
	Heart	0,544	2,5
40	Skin	3,821	6
	Rib	1,591	6
	Heart	0,457	2,5
45	Skin	3,802	6
	Rib	1,446	6
	Heart	0,368	2,5

CONCLUSION

- Maximum flux reached from 5 to 9 cm from liver surface.
- Irradiating time to kill cancer tissue from 9 min 45 sec until 19 min 54 sec.
- Maximum of boron-10 concentration for liver tissue is 47 μg/g cancer tissue and need 9 min 45 sec for therapy.
- The depth of tissue which has the most optimum thermal neutron flux is located in the range of 1,5 to 2,0 cm from the surface; i.e. skin. In that range, thermal neutron flux has its peak,

- Irradiation time needed to irradiate lung carcinoma will decrease simultaneously with the increasing number of boron-10 concentration in tumor. Irradiation time needed to combat and eradicate cancerous cell in this study is in the range of 219,840 minutes to 375,342 minutes,
- The most optimum number of boron-10 concentration in this particular case is 45 μg/g tumor tissue. With 45 μg/g tumor tissue, the optimum dose in the tumor is obtained while organs at risk were still kept under their Normal Tissue Tolerances.

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